SUPPORT FOR THE AMENDMENTS

The present amendment cancels claims 1-9, and adds new claims 10-21.

Support for newly added claims 10 and 13-21 is found at specification page 4, lines 6-11, 22-24 and 30, and page 5, lines 1-3, as well as original claims 1 and 4-9.

Support for newly added claims 11 and 12 is found at specification page 5, lines 29-30, as well as original claims 2 and 3.

It is believed that these amendments have not resulted in the introduction of new matter.

REMARKS

Claims 10-21 are currently pending in the present application. Claims 1-9 have been cancelled, and new claims 10-21 have been added, by the present amendment.

The rejection of now cancelled claims 1-9 under 35 U.S.C. § 103(a) as being obvious over Ferrari (U.S. 6,846,950) in view of Solomons (T.W.G. Solomons, Organic Chemistry, 5th Edition, John Wiley & Sons, Inc., pp. 762-764 (1992)) is respectfully traversed with respect to new claims 10-21.

New claim 10 recites a process for the preparation of gabapentin which comprises: Hofmann rearrangement of 1,1-cyclohexanediacetic acid monoamide to produce a reaction mixture; and precipitation of 1-(aminomethyl)cyclohexaneacetic acid (a.k.a., gabapentin) from the reaction mixture by acidification of the reaction mixture to a pH of from 4 to 6.3 by the addition of organic acid, inorganic acid, or a mixture thereof.

Unlike the claimed invention, Ferrari describes a *fundamentally different process* for the preparation of gabapentin which comprises: reaction of 1,1-cyclohexanediacetic acid with a mixture of acetic anhydride and ammonium acetate to produce 3,3-pentamethylene glutarimide (a.k.a., 3-azaspiro[5.5]-undecane-2,4-dione); treatment of 3,3-pentamethylene glutarimide with sodium hydroxide in an aqueous solution up to dissolution; dripping the aqueous solution into an aqueous mixture of sodium hydroxide and sodium hypochlorite; acidification of the aqueous solution with hydrochloric acid to produce 1-(aminomethyl)cyclohexaneacetic acid hydrochloride (a.k.a., gabapentin hydrochloride); and conversion of gabapentin hydrochloride to gabapentin by treatment of gabapentin hydrochloride with dicyclohexylamine.

Unlike the claimed invention, Solomons merely describes acid dissociation constants (pKa's) for various carboxylic acids.

The mere possibility that the process described in Ferrari could be modified to arrive at the claimed process is an insufficient ground for arriving at a supportable conclusion of

unpatentability. A *prima facie* case of obviousness requires that the prior art provide a skilled artisan with sufficient motivation and guidance to stop and make the proposed changes to the reference synthesis in order to arrive at the claimed process. Solomons merely describes acid dissociation constants (pKa's) for various carboxylic acids. Accordingly, Solomons fails to provide a skilled artisan with sufficient motivation and guidance to stop and make the proposed changes to the reference synthesis of Ferrari in order to arrive at the claimed process, absent impermissible hindsight reconstruction. Therefore, Ferrari and Solomons, when considered alone or in combination, fail to provide sufficient motivation and guidance to direct a skilled artisan to stop and modify the process described in Ferrari with a reasonable expectation of arriving at the claimed process for successfully preparing gabapentin.

Assuming *arguendo* that sufficient motivation and guidance is considered to have been provided by Ferrari and Solomons, which is not the case, such a case of obviousness is rebutted by a showing of secondary considerations.

As discussed in the present specification, conventional processes for preparing gabapentin, including the process described in Ferrari, require the conversion of gabapentin hydrochloride to gabapentin, which involves an additional time consuming synthetic step that employs expensive purification equipment and generates enormous amounts of liquid waste, thereby necessitating environmental countermeasures and increasing production costs (See e.g., page 2, last line, page 3, lines 1-30, page 4, line 1). Accordingly, there has been a long-felt need to reduce production costs during processes for preparing gabapentin while minimizing the negative impact that the generation of enormous amounts of liquid waste has on the environment. Based on the conventional process for preparing gabapentin described in Ferrari, and the limited disclosure provided by Solomons, other skilled artisans have failed to discover a solution to this long-felt need.

In contrast however, Applicants have discovered a low-cost process for directly preparing gabapentin without requiring the additional synthetic step and corresponding equipment of converting gabapentin hydrochloride to gabapentin employed by conventional processes, including the process described in Ferrari, thereby lowering production costs and minimizing the negative impact that the generation of enormous amounts of liquid waste has on the environment (See e.g., page 7, lines 1-17). Had the claimed process been obvious to a skilled artisan, Ferrari would have described the same in order to minimize the number of synthetic steps required to prepare gabapentin and thereby lower production costs and minimize the negative impact that liquid waste has on the environment.

Withdrawal of this ground of rejection is respectfully requested.

In conclusion, Applicants submit that the present application is now in condition for allowance and notification to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

David P. Stitzel
Attorney of Record
Registration No. 44,360

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 06/04)